

### **ABSTRACT OF THE DISCLOSURE**

Peptide inhibitors of glycogen synthase kinase-3 (GSK-3) having an amino acid sequence motif of XZXXXS(p)X, wherein S(p)=phosphorylated serine or phosphorylated threonine, X=any amino acid, and Z=any amino acid except serine or threonine. These inhibitors, which are about 7 to 20 amino acids long, are specific for GSK-3 and strongly inhibit the enzyme with an IC<sub>50</sub> of about 150  $\mu$ M. Also provided are methods of treating biological conditions mediated by GSK-3 activity, such as potentiating insulin signaling in a subject, treating or preventing type 2 diabetes in a patient, and treating Alzheimer's Disease by administering peptide inhibitors. Compositions of these peptide inhibitors and pharmaceutically acceptable carriers are also provided, as is a method for identifying inhibitors of GSK-3. The invention further relates to a computer-assisted method of structure based drug design of GSK-3 inhibitors using a three-dimensional structure of a peptide substrate of GSK-3.